Inside This Issue of JACC

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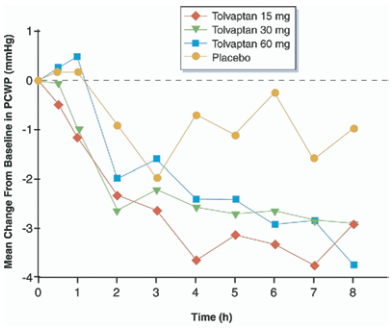
State-of-the-Art Paper

Defining the Cardiorenal Syndrome

The simplistic view of cardiorenal syndrome (CRS) is that a relatively normal kidney is dysfunctional because of a diseased heart. Ronco and colleagues offer a more sophisticated definition of CRS to incorporate the vast array of inter-related derangements and to stress the bidirectional nature of the interaction. Five subtypes of CRS are defined. Understanding the pathophysiological mechanisms underlying each subtype can help to provide a rationale for management strategies. **See page 1527. See figure.**



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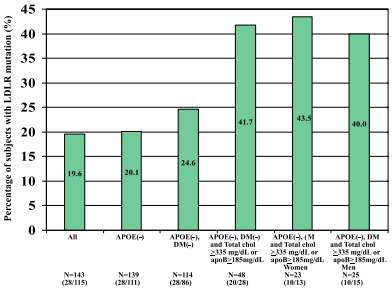
Clinical Trial

Tolvaptan Reduces Wedge Pressure and Increases Urine Output

Udelson and colleagues randomized almost 200 patients with heart failure (HF) and elevated filling pressures to a single dose of tolvaptan or placebo and then monitored their hemodynamics for up to 12 h. Tolvaptan reduced pulmonary capillary wedge pressure, right atrial pressure, and pulmonary artery pressure, and increased urine output compared to placebo. These data provide mechanistic support for the symptomatic improvements noted with tolvaptan in patients with decompensated HF. **See page 1540. See figure.**



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Lipid Disorders

Mutated *LDLR* Common in Patients Thought to Have FCH

Civeira and colleagues used a microarray that analyzes for 203 mutations in the low-density lipoprotein receptor (*LDLR*) gene and 4 defects in the apoplipoprotein E (*APOE*) gene to investigate unrelated patients with a clinical diagnosis of familial combined hypercholesterolemia (FCH). Approximately 20% of these patients had a mutation, and a total of 22 different mutations were found. Those with a mutation were more likely to have apolipoprotein B (apoB) levels >335 mg/dl or low-density lipoprotein (LDL) >185 mg/dl. Significant elevations in apoB or LDL, even if triglycerides are also elevated, may indicate a mutation in LDL and a diagnosis of familial hypercholesterolemia (FH), rather than FCH. **See pages 1546 and 1554. See figure.**

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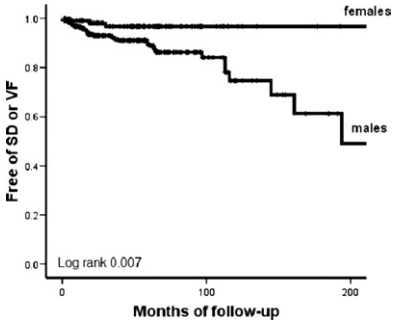
Antiplatelet Therapy

CCBs May Reduce the Efficacy of Clopidogrel

Clopidogrel is a pro-drug that requires hepatic bioactivation by the cytochrome P450 isoform 3A4. Most calcium-channel blockers (CCBs) are metabolized by the same enzyme to inactive metabolites. Siller-Matula and colleagues report that the platelet reactivity index was higher, that is, less inhibited, in patients who were taking both a CCB and clopidogrel compared to those only taking a clopidogrel blocker. Coadministration of CCBs and clopidogrel may result in decreased efficacy of clopidogrel. **See pages 1557 and 1564. See figure.**



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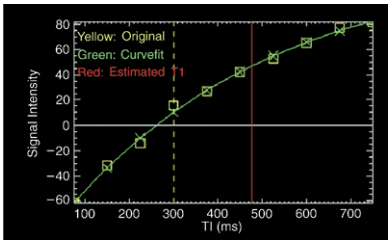
Heart Rhythm Disorders

Males Are More Symptomatically Affected by Brugada Syndrome

Benito and colleagues analyzed 384 patients with Brugada syndrome (approximately two-thirds male) to assess differences in clinical phenotype and prognosis according to gender. Males presented more frequently with symptoms, were more likely to have inducible ventricular fibrillation (VF), and were more likely to have sudden death or VF during follow-up. However, conduction parameters and corrected QT interval after exposure to sodium-channel blockers increased more in females. These results highlight the significant effect of gender on clinical outcomes in patients with Brugada syndrome. **See page 1567. See figure.**



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Cardiac Imaging

CMR Can Quantify Diffuse Myocardial Fibrosis

Regional myocardial fibrosis can be identified with delayed contrast enhancement on cardiac magnetic resonance imaging (deCMR). However, this technique relies on differences between scarred and normal myocardium, limiting its ability to diagnose diffuse processes. Iles and colleagues developed a technique to calculate a global post-contrast myocardial T_1 time as an index of diffuse fibrosis. This technique was validated in a series of experiments including comparisons to endomyocardial biopsy specimens and echocardiographic measurements of myocardial stiffness. This technique appears to be a valid method for identifying diffuse myocardial fibrosis. **See pages 1574 and 1581. See figure.**

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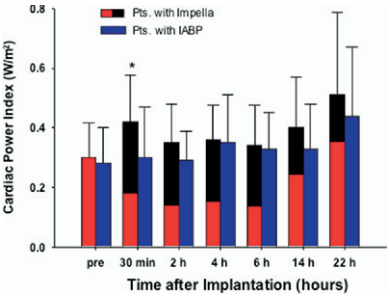

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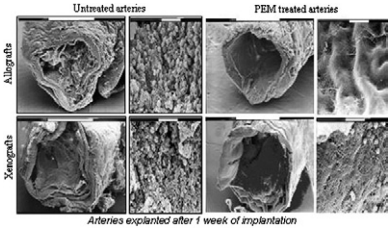

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Works in Progress

Percutaneous LVAD Restores Cardiac Output More Quickly Than IABP

The Impella LP2.5 is a percutaneously-delivered left ventricular assist device (LVAD) that is placed retrogradely into the left ventricle and pumps blood at up to 2.5 l/min to the ascending aorta. Seyfarth and colleagues assigned 26 patients with cardiogenic shock secondary to acute myocardial infarction to either the LVAD or to an intra-aortic balloon pump (IABP). Those assigned to LVAD had greater improvements in cardiac index and mean arterial pressure. Larger trials will be needed to assess the impact on clinical outcomes, but this LVAD appears promising for patients with cardiogenic shock. **See page 1584. See figure.**

Pre-Clinical Research

Polyelectrolyte Film Treatment May Extend Life of Arterial Conduit Grafts

Kerdjoudj and colleagues have shown that treating arteries that have been de-endothelialized with alternating layers of polyanions and polycations can form a polyelectrolyte multilayer film (PEM) that is both biocompatible and bioinert. For this in vivo study, human umbilical arteries were treated with PEM and used as bypass grafts for rabbit carotids. Follow-up included serial ultrasound evaluations and histological examination. All PEM-coated conduits were patent and had clean luminal surfaces at up to 12 weeks of follow-up. This study suggests that human umbilical arteries treated with PEM may constitute a useful option for bypassing small arteries. **See page 1589. See figure.**